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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/530,818 | 01/09/2002 | David R. Elmaleh | MGA-004.25 | 2433 |

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| EXAMINER | |
|---|---|
| JONES, DAMERON LEVEST | |
| **ART UNIT** | **PAPER NUMBER** |
| 1618 | |

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/530,818 | ELMALEH ET AL. | |
| | Examiner | Art Unit | |
| | D. L. Jones | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 8-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the response filed 5/6/05 wherein claims 1, 9, and 12 are amended and claims 2-7 and 3-18 are canceled.

***Note***: Claims 1 and 8-12 are pending.

## RESPONSE TO APPLICANT'S ELECTION

2. Applicant's has elected to prosecute Group X in the response filed 5/6/05 with traverse. The traversal is on the basis that simultaneous examination of the full scope of the instant invention would not place a serious burden on the .Examiner event though it includes claims to independent or distinct inventions.

Applicant's arguments are found non-persuasive because a separate search of each group is necessary. In addition, it is noted that prior art which anticipates or renders obvious a clotting component targeting moiety would neither anticipate nor render obvious targeting moieties selected from cells (including muscle cells, macrophages, foam cells, monocytes, polymorphonuclear cells, cellular fragments), colony stimulating factors, platelet factor 4, growth factors, cytokines, interferons, tumor necrosis factors, cellular sources of energy for metabolic active plaque formation, lipids, or lipid receptors. As a result, a serious burden on the Examiner is necessary since a separate search of the art is necessary for each distinct invention. Thus, the restriction is deemed proper and is made FINAL.

**112 FIRST PARAGRAPH REJECTIONS (Scope of Enablement)**

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 and 8-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for clotting components selected from fibrin, thrombin, fibrinogen, factor V III, and factor IX as set forth on page 3, lines 21-22 of the specification, does not reasonably provide enablement for all components of clotting. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are (1) nature of the invention; (2) state of the prior art; (3) level of one of ordinary skill in the art; (4) level of predictability in the art; (5) amount of direction and guidance provided by the inventor; (6) existence of working examples; (7) breadth of claims; and (8) quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(1) Nature of the invention

The claims are directed to an imaging agents, method of imaging using the agent, and kit comprising the imaging agent wherein the agent comprises a radionuclide and targeting moiety wherein the targeting moiety is a component of clotting and the radionuclide is selected from 18F, 68Ga, and 62Cu, or radioactive isotopes of iodine.

(2) State of the prior art

The references of record do not indicate all possible clotting components that useful with the claimed invention.

(3) Level of one of ordinary skill in the art

The level of one of ordinary skill in the art is high. Independent claims 1, 9, and 12 encompass a vast number of possible clotting components. Applicant's specification does not enable the public to make or use such a vast number of possible clotting components used in combination with the desired radionuclides.

(4) Level of predictability in the art

The art pertaining to clotting components is highly unpredictable because of the number of possible components. Determining the various types of components or class of components that may be radiolabeled and used as a cardiovascular imaging agent requires various experimental procedures and without guidance that is applicable to all clotting components, there would be little predictability in performing the claimed invention.

(5) Amount of direction and guidance provided by the inventor

Independent claims 1, 9, and 12 encompass a vast number of clotting components. Applicant's limited guidance does not enable the public to prepare such a

numerous amount of clotting components-radionuclide combinations. There is no directional guidance for the all the possible clotting components that will be useful for cardiovascular imaging once radiolabeled. Hence, there is no enablement for all possible permutations and combinations of the clotting component-radionuclide complex.

(6) Existence of working examples

Independent claims 1, 9, and 12 encompass a vast number of imaging agents. Applicant's limited working examples do not enable the public to prepare such a numerous amount of clotting components-radionuclide complexes. While Applicant's claims encompass a plethora of clotting components-radionuclide complexes, the specification does not provide an examples in which clotting agents are radiolabeled and used as cardiovascular imaging agents.

(7) Breadth of claims

The claims are extremely broad due to the vast number of possible clotting components-radionuclide complexes known to exist.

(8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims. In particular, the specification fails to enable the skilled artisan to practice the invention without undue experimentation. Furthermore, based on the unpredictable nature of the invention, the

state of the prior art, and the extreme breadth of the claims, one skilled in the art could not perform the claimed invention without undue experimentation.

**112 SECOND PARAGRAPH REJECTIONS**

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1 and 8-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims as written are ambiguous because it is unclear what components of clotting Applicant is claiming that are compatible with the instant invention. Applicant is respectfully requested to clarify the instant invention in order that one may readily ascertain what is being claimed.

**103 REJECTIONS**

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1 and 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg (US Patent No. 5,364,612) in view of Calenoff (US Patent No. 6,025,477).

**Goldenberg** discloses reagents, methods of detecting and imaging cardiovascular lesions (i.e., atherosclerosis, vascular clots, etc.), and kits thereof wherein an antibody imaging agent specific for antigens associated with fibrin may be used (see entire document, especially, abstract; column 3, lines 62-68; column 4, lines 1-8; columns 9-10, bridging paragraph). The conjugates may be monospecific, bispecific, trispecific, or multispecific antibodies conjugated to an imaging radioisotope (column 6, lines 5-11). The antibody conjugate may be labeled with a radioisotope using any conventional method (column 10, lines 34-54; column 11, lines 6-12). In Example 3, column 17, cardiovascular imaging is disclosed. In Example 4, column 17, scintigraphic imaging kit is disclosed. In Example 5, column 17, diagnostic imaging of myocardial infarction is disclosed. While Goldenberg discloses a cardiovascular imaging agent, kit comprising an imaging agent, and a method of imaging cardiovascular plaques, the reference fails to disclose all possible radioisotopes that be conjugated to the cardiovascular imaging agent.

**Calenoff** discloses the detection of atherosclerotic plaques using an imaging agent (see entire document, especially, abstract column 14, lines 62-68; column 15, lines 22-28; column 16, lines 8-13). Antibodies bind to the atherosclerotic plaque antigen. The antibody is labeled with a detectable marker that is selected depending upon the application desired. The choice of marker is readily determinable to one

skilled in the art (column 8, lines 8-13; column 15, lines 52-59). In addition, Calenoff discloses a method of quantitatively determining the antibody concentration in a sample (columns 11-12, bridging paragraph; column 12, lines 20-38; columns 12-13, bridging paragraph; column 14, lines 4-25). It is noted that in the technique of columns 12-13, bridging paragraph, for example, that the quantitative determination of the concentration of the labeled antigen may be detected. Radioisotopes that are commonly used in medicine and well known to those in the art include 123I, 125I, 128I, 131I, gallium-68, and copper II isotopes (column 15, lines 5-21). The invention of Calenoff enables one to monitor the progression of atherosclerosis (column 15, lines 60-68). Possible imaging techniques include PET, x-ray, CAT scan, NMRI, and fluoroscopy (column 16, lines 29-32).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Goldenberg using the teachings of Calenoff and generate a cardiovascular imaging agent, kit, and method of imaging cardiovascular plaques as set forth in independent claims 1,9, and 12 wherein a clotting component of fibrin in combination with a radionuclide are utilized for the following reasons. (1) Goldenberg discloses a multispecific imaging agent antibody conjugate that is specific for at least two different antigens that include fibrin. (2) Goldenberg discloses that the radioisotope conjugated to the targeting moiety is dependent upon the imaging technique desired. (3) Goldenberg discloses diagnostic imaging of cardiovascular lesion using its conjugates (e.g., see claims 1 and 13 in column 18 of Goldenberg). (4) Goldenberg discloses that diagnostic imaging kits may be generated

using the cardiovascular imaging agents (e.g., see Example 4, column 17, and claims 42-45 of Goldenberg). (5) While Goldenberg fails to disclose all possible radioisotopes that may be used with the cardiovascular imaging agents, Calenoff discloses radioactive isotopes that are commonly used in medicine and are well known to those in the art (Calenoff, column 15, lines 5-28). Possible radioisotopes for cardiovascular imaging agents include Ga-68, copper (II) isotopes, and iodine isotopes, preferably 123I, 125I, 128I, and 131I. In addition, Calenoff discloses that PET is one of the possible imaging techniques by which the isotopes may be analyzed. Hence, since both Goldenberg and Calenoff are directed to cardiovascular imaging agents, a skilled practitioner in the art would be motivate to combine the teachings of the references since they are in the same field of endeavor.

**COMMENTS/NOTES**

9. Applicant is respectfully requested to cancel all non-elected subject matter.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. L. Jones
Primary Examiner
Art Unit 1618

July 21, 2005